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=> s l1 and signal

L2 224 L1 AND SIGNAL

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L3 94 L2 AND TRANSPO?

=> s l3 and pore?

L4 0 L3 AND PORE?

=> s l3 and peptide

L5 52 L3 AND PEPTIDE

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=> dup rem l6

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L7 13 DUP REM L6 (4 DUPLICATES REMOVED)

=> d l7 ibib abs

L7 ANSWER 1 OF 13 MEDLINE
ACCESSION NUMBER: 1999218283 MEDLINE
DOCUMENT NUMBER: 99218283
TITLE: The membrane-attached electron carrier cytochrome cy from Rhodobacter sphaeroides is functional in respiratory but not in photosynthetic electron transfer.
AUTHOR: Myllykallio H; Zannoni D; Daldal F
CORPORATE SOURCE: Department of Biology, Plant Science Institute, University of Pennsylvania, Philadelphia, PA 19104-6018, USA.
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1999 Apr 13) 96 (8) 4348-53. Journal code: PV3. ISSN: 0027-8424.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199907
ENTRY WEEK: 19990704

AB Rhodobacter species are useful model organisms for studying the structure and function of c type cytochromes (Cyt c), which are ubiquitous electron carriers with essential functions in cellular energy and **signal** transduction. Among these species, Rhodobacter capsulatus has a periplasmic Cyt c2Rc and a membrane-bound bipartite Cyt cyRc. These electron carriers participate in both respiratory and photosynthetic electron-transfer chains. On the other hand, until recently, Rhodobacter sphaeroides was thought to have only one of these two cytochromes, the soluble Cyt c2Rs. Recent work indicated that this species has a gene, cycYRs, that is highly homologous to cycYRc, and in the work presented here, functional properties of its gene product (Cyt cyRs) are defined. It was found that Cyt cyRs is unable to participate in photosynthetic electron transfer, although it is active in respiratory electron transfer, unlike its R. capsulatus counterpart, Cyt cyRc. **Chimeric** constructs have shown that the photosynthetic incapability of Cyt cyRs is caused, at least in part, by its redox active subdomain, which carries the covalently bound heme. It, therefore, seems that this domain interacts differently with distinct redox partners, like the photochemical reaction center and the Cyt c oxidase, and allows the bacteria to funnel electrons efficiently to various destinations under different growth conditions. These findings raise an intriguing evolutionary issue in regard to cellular apoptosis: why do the **mitochondria** of higher organisms, unlike their bacterial ancestors, use only one soluble electron carrier in their respiratory electron-**transport** chains?

=> d l7 ibib abs tot

L7 ANSWER 1 OF 13 MEDLINE
ACCESSION NUMBER: 1999218283 MEDLINE
DOCUMENT NUMBER: 99218283
TITLE: The membrane-attached electron carrier cytochrome cy from Rhodobacter sphaeroides is functional in respiratory but not in photosynthetic electron transfer.
AUTHOR: Myllykallio H; Zannoni D; Daldal F
CORPORATE SOURCE: Department of Biology, Plant Science Institute, University of Pennsylvania, Philadelphia, PA 19104-6018, USA.
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1999 Apr 13) 96 (8) 4348-53. Journal code: PV3. ISSN: 0027-8424.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199907
ENTRY WEEK: 199[redacted]04

AB Rhodobacter species are useful model organisms for studying the structure and function of c type cytochromes (Cyt c), which are ubiquitous electron carriers with essential functions in cellular energy and **signal** transduction. Among these species, Rhodobacter capsulatus has a periplasmic Cyt c2Rc and a membrane-bound bipartite Cyt cyRc. These electron carriers participate in both respiratory and photosynthetic electron-transfer chains. On the other hand, until recently, Rhodobacter sphaeroides was thought to have only one of these two cytochromes, the soluble Cyt c2Rs. Recent work indicated that this species has a gene, cycYRs, that is highly homologous to cycYRc, and in the work presented here, functional properties of its gene product (Cyt cyRs) are defined. It was found that Cyt cyRs is unable to participate in photosynthetic electron transfer, although it is active in respiratory electron transfer, unlike its R. capsulatus counterpart, Cyt cyRc. **Chimeric** constructs have shown that the photosynthetic incapability of Cyt cyRs is caused, at least in part, by its redox active subdomain, which carries the covalently bound heme. It, therefore, seems that this domain interacts differently with distinct redox partners, like the photochemical reaction center and the Cyt c oxidase, and allows the bacteria to funnel electrons efficiently to various destinations under different growth conditions. These findings raise an intriguing evolutionary issue in regard to cellular apoptosis: why do the **mitochondria** of higher organisms, unlike their bacterial ancestors, use only one soluble electron carrier in their respiratory electron-**transport** chains?

L7 ANSWER 2 OF 13 MEDLINE
ACCESSION NUMBER: 1999168219 MEDLINE
DOCUMENT NUMBER: 99168219
TITLE: Phylogenetic transfer of organelle genes to the **nucleus** can lead to new mechanisms of protein integration into membranes.
AUTHOR: Michl D; Karnauchov I; Berghofer J; Herrmann R G; Klosgen R B
CORPORATE SOURCE: Botanisches Institut der Ludwig-Maximilians-Universitat, Munchen, Germany.
SOURCE: PLANT JOURNAL, (1999 Jan) 17 (1) 31-40. Journal code: BRU. ISSN: 0960-7412.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199906
ENTRY WEEK: 19990601

AB Subunits CFo-I and CFo-II of ATP synthase in **chloroplast** thylakoid membranes are two structurally and functionally closely related proteins of bitopic membrane topology which evolved from a common ancestral gene. In higher plants, CFo-I still originates in plastid chromosomes (gene: atpF), while the gene for CFo-II (atpG) was phylogenetically transferred to the **nucleus**. This gene transfer was accompanied by the reorganization of the topogenic signals and the mechanism of membrane insertion. CFo-I is capable of integrating correctly as the mature protein into the thylakoid membrane, whereas membrane insertion of CFo-II strictly depends on a hydrophobic targeting **signal** in the transit **peptide**. This requirement is caused by three negatively charged residues at the N-terminus of mature CFo-II which are lacking from CFo-I and which have apparently been added to the protein only after gene transfer has occurred. Accordingly, the

CFo-II transit **peptide** is structurally and functionally equivalent to typical bipartite transit peptides, capable of also translocating hydrophilic lumenal proteins across thylakoid membrane. In this case, **transport** takes place by the Sec-dependent pathway, despite the fact that membrane integration of CFo-II is a Sec-independent, and presumably spontaneous, process.

L7 ANSWER 3 OF 13 MEDLINE
ACCESSION NUMBER: 1999030358 MEDLINE
DOCUMENT NUMBER: 99030358
TITLE: Protein **transport** into "complex" diatom plastids utilizes two different targeting signals.
AUTHOR: Lang M; Apt K E; Kroth P G
CORPORATE SOURCE: Institut fur Biochemie der Pflanzen, Heinrich-Heine-Universitat Dusseldorf, Universitatsstrasse 1, D-40225 Dusseldorf, Germany.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 Nov 20) 273 (47) 30973-8.
Journal code: HIV. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199902
ENTRY WEEK: 19990204

AB The plastids found in diatoms and other chromophytic algae are completely enclosed by four membranes in contrast to **chloroplasts** of higher plants, which are surrounded by only two membranes. The bipartite targeting sequence of diatom **nuclear**-encoded plastid proteins contains an endoplasmic reticulum **signal** sequence and, based on sequence comparison, a transit **peptide**-like domain similar to that which targets proteins into the plastids of higher plants. By performing heterologous import experiments using the precursor of the gamma subunit of the **chloroplast** ATPase from the diatom Odontella sinensis we were able to show that protein import into diatom plastids is at least a two-step event. We demonstrate that the first step involves co-translational **transport** through endoplasmic reticulum membranes and that there is an additional targeting step which is similar to the import of precursor proteins into **chloroplasts** of higher plants and green algae indicating that the transit **peptide**-like domain of the diatom precursor is functionally equivalent to the respective targeting **signal** of higher plants. Our results suggest that the transit **peptide** depending targeting mechanism in plastids has apparently remained relatively unchanged over the course of evolution, with only the peptidase cleavage site significantly modified.

L7 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1997:476311 CAPLUS
DOCUMENT NUMBER: 127:92186
TITLE: Recombinant preparation of ubiquinones in Saccharomyces cerevisiae by using heterologous prenyl transferase
INVENTOR(S): Matsuda, Hideyuki; Kawamuki, Makoto; Nakagawa, Tsuyoshi
PATENT ASSIGNEE(S): Alpha Shokuhin K. K., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 09173076	A2	19970708	JP 1995-351243	19951227

AB Disclosed is a method for the prodn. of ubiquinones in Saccharomyces cerevisiae via the expression of a fusion protein consisting of the **peptide** assocd. with the **mitochondrial transportation** of hexprenyl diphosphate synthase (gene COQ1) of S. cerevisiae and a heterologous hexprenyl prenyl transferase encoded by gene ispB of Escherichia coli or the decaprenyl diphosphate synthase-encoding gene of S. pombe. Plasmid pYE6 was prepd. by inserting into shuttle vector YEp13M4 a **chimeric** gene of the DNA encoding the N-terminal 53 amino acids of S. cerevisiae gene COQ1 and the E. coli gene ispB. Use of the S. cerevisiae transformed with pYE6 for the prodn. of ubiquinone 8 and 6 was claimed. Cloning of gene for decaprenyl diphosphate synthase from S. pombe was also shown.

L7 ANSWER 5 OF 13 MEDLINE
ACCESSION NUMBER: 97390061 MEDLINE
DOCUMENT NUMBER: 97390061
TITLE: Immunocytochemical analysis of **peptide** hormone processing: importance of the positively charged N-terminal domain of **signal peptide** in correct ER targeting in yeast cells.
AUTHOR: Cheong K H; Park S D; Kim J; Hong S H
CORPORATE SOURCE: Department of Molecular Biology and Research Center for Cell Differentiation, College of Natural Sciences, Seoul National University, Korea.
SOURCE: CELL STRUCTURE AND FUNCTION, (1997 Jun) 22 (3) 365-77. Journal code: CSF. ISSN: 0386-7196.
PUB. COUNTRY: Japan
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199711
ENTRY WEEK: 19971103
AB We used a morphological approach to determine the topogenic role of the **signal peptide** in mediating the ER translocation of yeast prepro-alpha-factor. In prepro-alpha-factor-somatostatin hybrids, changes in the N-terminal amino acid sequence from wild-type NH2-Met-Arg-Phe (MRF) to NH2-Met-Phe-Lys (MFK) caused a subtle difference in protein trafficking in yeast cells. Immunofluorescence microscopy on semithin cryosections and immunoelectron microscopy on ultrathin sections showed that the **transposition** of the charged amino acid at N-terminus caused the precursors to be associated with either **nucleus** or **mitochondria**. This suggests that the secretory proteins are mistargeted to the irrelevant organelles as the result of inefficient ER translocation. Structural aspects of **nuclear** or **mitochondrial** targeting proteins and common principles in membrane translocation systems account for the mistargeting of overexpressed mutant hybrid precursors that are not rapidly translocated into the ER. Based on our immunocytochemical study on individual cells, we propose here that the positively charged N-terminal domain of **signal peptide** is important not merely in the efficiency of ER translocation, but also in appropriate targeting of **peptide** hormone precursors in yeast cells where post-translational ER translocation is known to occur frequently.

L7 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1995:792849 CAPLUS
DOCUMENT NUMBER: 123:220296
TITLE: Method for preparation of conjugates of **signal** peptides and **nucleic** acid fragments and their use in targeting **nucleic** acids in cells and cell organelles
INVENTOR(S): Seibel, Peter; Seibel, Andrea
PATENT ASSIGNEE(S): Germany
SOURCE: Ger., 19 pp.

CODEN: GWXXAW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4421079	C1	19950817	DE 1994-4421079	19940616
DE 19520815	A1	19951221	DE 1995-19520815	19950611
DE 19520815	C2	19960725		
WO 9534665	A2	19951221	WO 1995-DE775	19950611
WO 9534665	A3	19960222		
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9526679	A1	19960105	AU 1995-26679	19950611
EP 774006	A2	19970521	EP 1995-921691	19950611
R: AT, BE, CH, DE, FR, GB, IE, IT, LI, LU, NL				

PRIORITY APPLN. INFO.: DE 1994-4421079 19940616
WO 1995-DE775 19950611

AB Linkage of a **nucleic** acid fragment to a **signal** sequence allows the **transport** of the **nucleic** acid sequence through the membrane to a specific target for use in gene therapy. In linking the **nucleotide** sequence to a **signal peptide**, natural protein **transport** pathways can be used for site-directed mutagenesis and for the mol. therapy of inherited diseases. The **nucleic** acid moiety of the conjugate may be synthesized chem., e.g. to incorporate **nuclease**-resistant phosphorothioate, or by transcription. A 39 **nucleotide** fragment is linked to the **signal** sequence of the rat **mitochondrial** ornithine carboxylase to achieve **transport** across the **mitochondrial** membrane. The oligonucleotide forms a hairpin loop and has a 5' overhang to which further **nucleic** acid sequences can be linked.

L7 ANSWER 7 OF 13 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 95386538 MEDLINE
DOCUMENT NUMBER: 95386538
TITLE: Sorting of **nuclear**-encoded **chloroplast** membrane proteins to the envelope and the thylakoid membrane.
AUTHOR: Brink S; Fischer K; Klosgen R B; Flugge U I
CORPORATE SOURCE: Botanisches Institut der Universitat zu Koln, Germany..
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1995 Sep 1) 270 (35) 20808-15.
Journal code: HIV. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199512

AB The spinach triose phosphate/phosphate translocator and the 37-kDa protein are both integral components of the **chloroplast** inner envelope membrane. They are synthesized in the cytosol with N-terminal extensions, the transit peptides, that are different in structural terms from those of imported stromal or thylakoid proteins. In order to determine if these N-terminal extensions are essential for the correct localization to the envelope membrane, they were linked to the mature parts of thylakoid membrane proteins, the light-harvesting chlorophyll a/b binding protein

and the CF0II-subunit of the thylakoid ATP synthase, respectively. In addition, the transit **peptide** of the CF0II-subunit that contains signals for the **tr[redacted]port** across both the envelope [redacted] the thylakoid membrane was fused to the mature parts of both envelope membrane proteins. The **chimeric** proteins were imported into isolated spinach **chloroplasts**, and the intraorganellar routing of the proteins was analyzed. The results obtained show that the N-terminal extensions of both envelope membrane proteins possess a stroma-targeting function only and that the information for the integration into the envelope membrane is contained in the mature parts of the proteins. At least part of the integration **signal** is provided by hydrophobic domains in the mature sequences since the removal of such a hydrophobic segment from the 37-kDa protein leads to missorting of the protein to the stroma and the thylakoid membrane.

L7 ANSWER 8 OF 13 MEDLINE
ACCESSION NUMBER: 95175350 MEDLINE
DOCUMENT NUMBER: 95175350
TITLE: Transfection of **mitochondria**: strategy towards a gene therapy of **mitochondrial** DNA diseases.
AUTHOR: Seibel P; Trappe J; Villani G; Klopstock T; Papa S; Reichmann H
CORPORATE SOURCE: Institute of Medical Biochemistry and Chemistry, Bari, Italy..
SOURCE: NUCLEIC ACIDS RESEARCH, (1995 Jan 11) 23 (1) 10-7. Journal code: O8L. ISSN: 0305-1048.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199506
AB Successes in classical gene therapies have been achieved by placing a corrected copy of a defective **nuclear** gene in cells. A similar gene replacement approach for a mutant **mitochondrial** genome is invariably linked to the use of a yet unavailable **mitochondrial** transfection vector. Here we show that DNA coupled covalently to a short **mitochondrial** leader **peptide** (**chimera**) can enter **mitochondria** via the protein import pathway, opening a new way for gene-, antisense-RNA- or antisense-DNA-delivery in molecular therapies. The import behavior of the purified **chimera**, composed of the amino-terminal leader **peptide** of the rat ornithine transcarbamylase (OTC) and a double stranded DNA molecule (17 bp or 322 bp), was tested by incubating with coupled and 'energized' rat liver **mitochondria** in the presence of reticulocyte lysate. The **chimera** was translocated with a high efficiency into the matrix of **mitochondria** utilizing the protein import pathway, independent from the size of its passenger DNA.

L7 ANSWER 9 OF 13 MEDLINE
ACCESSION NUMBER: 95105170 MEDLINE
DOCUMENT NUMBER: 95105170
TITLE: The thylakoid translocation of subunit 3 of photosystem I, the psaF gene product, depends on a bipartite transit **peptide** and proceeds along an azide-sensitive pathway.
AUTHOR: Karnauchov I; Cai D; Schmidt I; Herrmann R G; Klosgen R B
CORPORATE SOURCE: Botanisches Institut, Ludwig-Maximilians-Universitat, M unchen, Federal Republic of Germany..
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1994 Dec 30) 269 (52) 32871-8. Journal code: HIV. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals

ENTRY MONTH: 199504
AB Subunit 3 of photosystem I (PSI-3), the product of the **nuclear** psaF gene, is the docking protein for plastocyanin during photosynthetic electron **transport** in thylakoid membranes and is synthesized in the cytosol with a transit **peptide** that resembles structurally the bipartite targeting signals of hydrophilic, lumenal components such as plastocyanin. In organello import experiments performed with the authentic PSI-3 precursor and **chimeric** polypeptides consisting of residue-correct fusions of transit peptides and mature proteins derived from different plastid proteins demonstrate that the PSI-3 transit **peptide** is indeed capable of translocating proteins into the thylakoid lumen and that, conversely, mature PSI-3 depends on a bipartite transit **peptide** for its thylakoid transfer. Of the three recently described translocation/integration pathways for **nucleus** -encoded proteins carrying bipartite transit peptides that are distinct in their physiological requirements and strictly protein-specific, PSI-3, like plastocyanin and the 33-kDa protein of the oxygen-evolving complex, is translocated by a pathway that involves stromal factors but no proton gradient across the membrane. It is not affected by saturating amounts of the precursor for the 23-kDa protein of the oxygen-evolving complex that follows the latter route. Thylakoid translocation of PSI-3 is, however, impaired in the presence of sodium azide, which indicates that a homolog to the bacterial SecA protein might be involved in this process suggesting, thus, a prokaryote-like translocation pathway. The azide-sensitive factor appears to interact predominantly with the transit **peptide** of a precursor protein, since **chimeras** consisting of a presequence from an azide-resistant precursor and a mature part of an azide-sensitive polypeptide are still translocated in the presence of the inhibitor.

L7 ANSWER 10 OF 13 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 94193697 MEDLINE
DOCUMENT NUMBER: 94193697
TITLE: Differences between lumen targeting domains of **chloroplast** transit peptides determine pathway specificity for thylakoid **transport**.
AUTHOR: Henry R; Kapazoglou A; McCaffery M; Cline K
CORPORATE SOURCE: Horticultural Sciences Department, University of Florida, Gainesville 32611..
CONTRACT NUMBER: 1 R01 GM46951 (NIGMS)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1994 Apr 8) 269 (14) 10189-92.
Journal code: HIV. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199407
AB **Nuclear** encoded thylakoid lumen proteins are imported into the **chloroplast** storma and further directed across thylakoid membranes by lumen targeting domains. Recently, we showed that there are two protein-specific pathways for **transport** into the lumen. This was unexpected in that lumen targeting domains have similar properties, all containing bacterial **signal peptide** motifs. Nevertheless, sequence homology analysis suggests that pathway specificity is determined by elements in the lumen targeting domain. To test this, we constructed and analyzed **chimeric** proteins in which transit peptides from proteins **transported** by one pathway were fused to the mature domains of proteins directed by the other. We also investigated the **transport** characteristics of a previously unexamined protein

whose pathway was predicted by sequence similarity analysis. Our results confirm that lumen targeting domains contain pathway sorting elements and further indicate that distinct energy and stroma requirements for **transport** are pathway characteristics, unrelated to the passenger protein. These findings suggest the operation of two mechanistically different translocators.

L7 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1993:468336 CAPLUS
DOCUMENT NUMBER: 119:68336
TITLE: The 20 kDa apoprotein of the CP24 complex of photosystem II: an alternative model to study import and intra-organellar routing of **nuclear**-encoded thylakoid proteins
AUTHOR(S): Cai, Daguang; Herrmann, Reinhold G.; Kloesgen, Ralf Bernd
CORPORATE SOURCE: Bot. Inst., Ludwig-Maximilians-Univ., Munich, 8000/19, Germany
SOURCE: Plant J. (1993), 3(3), 383-92
CODEN: PLJUED; ISSN: 0960-7412
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In organello assays were performed with isolated intact **chloroplasts** and the authentic precursor of the 20 kD apoprotein from spinach, or appropriate **chimeric** polypeptides consisting of a transit **peptide** and the mature part of various **nuclear**-encoded thylakoid proteins of known location and targeting epitopes, to resolve the characteristics of its targeting properties, as well as to det. the contribution of the individual parts of the precursor mol. to its import and subsequent intraorganellar routing. Expts. demonstrated that the transit **peptide** of the CP24 apoprotein is required only for the import of the protein into the organelle. All subsequent steps, such as the integration of the protein into the thylakoid membrane, binding of chlorophyll, assembly into the CP24 complex and migration to the grana lamellae, still take place if the authentic transit **peptide** is replaced by a targeting **signal** of a **nuclear**-encoded stromal protein.

L7 ANSWER 12 OF 13 MEDLINE
ACCESSION NUMBER: 86272084 MEDLINE
DOCUMENT NUMBER: 86272084
TITLE: The role of the transit **peptide** in the routing of precursors toward different **chloroplast** compartments.
AUTHOR: Smeekens S; Bauerle C; Hageman J; Keegstra K; Weisbeek P
CONTRACT NUMBER: HD7118 (NICHD)
SOURCE: CELL, (1986 Aug 1) 46 (3) 365-75.
Journal code: CQ4. ISSN: 0092-8674.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198611
AB The role of the transit **peptide** in the routing of imported proteins inside the **chloroplast** was investigated with **chimeric** proteins in which the transit peptides for the **nuclear**-encoded ferredoxin and plastocyanin precursors were exchanged. Import and localization experiments with a reconstituted **chloroplast** system show that the ferredoxin transit **peptide** directs mature plastocyanin away from its correct location, the thylakoid lumen, to the stroma. With the plastocyanin transit **peptide**-mature ferredoxin **chimera**, a processing intermediate is arrested on its way to the lumen. We propose a two domain hypothesis for the plastocyanin transit **peptide**: the

first domain functions in the **chloroplast** import process, whereas the second is responsible for **transport** across the thylakoid membrane. Thus, the transit **peptide** not only targets proteins to the **chloroplast**, but also is a major determinant in their subsequent localization within the organelle.

L7 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1985:161451 CAPLUS
DOCUMENT NUMBER: 102:161451
TITLE: Targeting of a foreign protein to **chloroplasts** by fusion to the transit **peptide** from the small subunit of ribulose 1,5-bisphosphate carboxylase
AUTHOR(S): Van den Broeck, Guido; Timko, Michael P.; Kausch, Albert P.; Cashmore, Anthony R.; Van Montagu, Marc; Herrera-Estrella, Luis
CORPORATE SOURCE: Lab. Genet., Rijksuniv. Gent, Ghent, B-9000, Belg.
SOURCE: Nature (London) (1985), 313(6001), 358-63
CODEN: NATUAS; ISSN: 0028-0836
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A **chimeric** gene was constructed which comprised the gene for the transit **peptide** of the precursor to the small subunit of the pea **chloroplast** ribulose 1,5-diphosphate carboxylase [9027-23-0] linked to the N-terminus of the bacterial neomycin phosphotransferase II (NPT-II) [53362-84-8] gene. The **chimeric** gene was placed under the control of the pea small subunit gene promoter, introduced into tobacco cells by Agrobacterium-mediated transformation, and the fate of the fusion protein that was synthesized in the transformed cells was studied. The NPT-II component of the fusion protein was translocated across the **chloroplast** envelope and into the stroma. The fusion protein underwent cleavage similar to that of the small subunit precursor.
The processing is performed by the same stromal **nuclease** which removes the transit **peptide** from the precursor to the small subunit polypeptide. Apparently, both translocation and processing occur efficiently for this novel precursor.

=> d history

(FILE 'HOME' ENTERED AT 17:04:26 ON 19 JUN 2000)

FILE 'MEDLINE, BIOSIS, CAPLUS, LIFESCI' ENTERED AT 17:04:39 ON 19 JUN 2000
L1 1773 S CHIMER? AND (MITOCHON? OR CHLOROPLAST?)
L2 224 S L1 AND SIGNAL
L3 94 S L2 AND TRANSPO?
L4 0 S L3 AND PORE?
L5 52 S L3 AND PEPTIDE
L6 17 S L5 AND NUCLE?
L7 13 DUP REM L6 (4 DUPLICATES REMOVED)

=> s l1 (p) nucle?

PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L1 (P) NUCLE?'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L2 (P) NUCLE?'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L3 (P) NUCLE?'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L4 (P) NUCLE?'
L8 748 L1 (P) NUCLE?

=> s nucle? (p)(mitochon? or chloroplast?)

L9 76417 NUCLE? (MITOCHON? OR CHLOROPLAST?)

=> s l9 and transpor?

L10 8522 L9 AND TRANSPOR?

=> l10 and signal

L10 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s l10 and signal

L11 512 L10 AND SIGNAL

=> s l11 and link?

L12 47 L11 AND LINK?

=> dup rem l12

PROCESSING COMPLETED FOR L12
L13 33 DUP REM L12 (14 DUPLICATES REMOVED)

=> d history

(FILE 'HOME' ENTERED AT 17:04:26 ON 19 JUN 2000)

FILE 'MEDLINE, BIOSIS, CAPLUS, LIFESCI' ENTERED AT 17:04:39 ON 19 JUN 2000
L1 1773 S CHIMER? AND (MITOCHON? OR CHLOROPLAST?)
L2 224 S L1 AND SIGNAL
L3 94 S L2 AND TRANSPO?
L4 0 S L3 AND PORE?
L5 52 S L3 AND PEPTIDE
L6 17 S L5 AND NUCLE?
L7 13 DUP REM L6 (4 DUPLICATES REMOVED)
L8 748 S L1 (P) NUCLE?
L9 76417 S NUCLE? (P)(MITOCHON? OR CHLOROPLAST?)
L10 8522 S L9 AND TRANSPOR?
L11 512 S L10 AND SIGNAL
L12 47 S L11 AND LINK?
L13 33 DUP REM L12 (14 DUPLICATES REMOVED)

=> s l13 not l7

L14 29 L13 NOT L7

=> d l14 ibib abs tot

L14 ANSWER 1 OF 29 MEDLINE
ACCESSION NUMBER: 1998417448 MEDLINE
DOCUMENT NUMBER: 98417448
TITLE: A regulatory factor, Fil1p, involved in derepression of the
isocitrate lyase gene in Saccharomyces cerevisiae--a possible mitochondrial protein necessary for protein synthesis in mitochondria.
AUTHOR: Kanai T; Takeshita S; Atomi H; Umemura K; Ueda M; Tanaka A
CORPORATE SOURCE: Department of Synthetic Chemistry and Biological Chemistry,

Graduate School of Engineering, Kyoto University, Japan.
SOURCE: EUROPEAN JOURNAL OF BIOCHEMISTRY, (1998 Aug 15) 256 (1) 212[redacted].
Journal code: EMZ. ISSN: 0014-2956.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
OTHER SOURCE: GENBANK-AB016033
ENTRY MONTH: 199812

AB A mutant was isolated that failed to derepress the 5' upstream region of Candida tropicalis isocitrate lyase gene (UPR-ICL)-mediated gene expression in acetate medium, and the gene (FIL1) that complemented this mutation was isolated. The fil1 null mutant in which FIL1 is disrupted (deltafil1 strain) could not grow on acetate or ethanol, and the derepression of the isocitrate lyase encoded by ICL1 in Saccharomyces cerevisiae was also defected. The amino acid sequence of Fil1p (230 amino acids) showed similarity to ribosome recycling factors (RRFs) of prokaryotes. Compared to prokaryotic RRFs, Fil1p had an N-terminal 46-amino-acid extension which was shown to be able to function as a **mitochondrial**-targeting sequence. The subcellular fractionation of the deltafil1 strain showed that protein constituents of the **mitochondrial** fraction of the deltafil1 strain differed from those of the wild-type strain, but resembled those of chloramphenicol-treated cells or rho(o) cells. The specific activity of cytochrome c oxidase, was severely decreased in deltafil1, rho(o) and chloramphenicol-treated cells compared with wild-type cells, while enzymatic levels of **mitochondrial** NAD+-**linked** isocitrate dehydrogenase, which is encoded by **nuclear** DNA, were not affected. These results suggest that Fillp is necessary for protein synthesis in **mitochondria** of S. cerevisiae. Furthermore, cells treated with antimycin A, along with chloramphenicol-treated, rho(o), and deltafil1 cells, showed deficiency in derepression of isocitrate lyase. Northern-blot analysis showed that this can be ascribed to no increase in transcription of ICL1 and FBP1 encoding fructose 1,6-bisphosphatase. The results indicate the presence of a communication pathway between **mitochondria** and the **nucleus** which represses expression of genes encoding the key enzymes of the glyoxylate cycle and gluconeogenic pathway when there is a deficiency in the **mitochondrial** respiratory chain.

L14 ANSWER 2 OF 29 MEDLINE
ACCESSION NUMBER: 1998284536 MEDLINE
DOCUMENT NUMBER: 98284536
TITLE: Cloning and chromosomal mapping of a novel ABC **transporter** gene (hABC7), a candidate for X-**linked** sideroblastic anemia with spinocerebellar ataxia.
AUTHOR: Shimada Y; Okuno S; Kawai A; Shinomiya H; Saito A; Suzuki M; Omori Y; Nishino N; Kanemoto N; Fujiwara T; Horie M; Takahashi E
CORPORATE SOURCE: Otsuka GEN Research Institute, Otsuka Pharmaceutical Company Ltd., Tokushima, Japan..
shim@gen.otsuka.genome.ad.jp
SOURCE: JOURNAL OF HUMAN GENETICS, (1998) 43 (2) 115-22.
Journal code: CYJ. ISSN: 1434-5161.
PUB. COUNTRY: Japan
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
OTHER SOURCE: GENBANK-AB005289
ENTRY MONTH: 199809

AB We isolated a novel human ATP-binding cassette (ABC) **transporter** cDNA, determined its **nucleotide** sequence, and designated it human ABC7 (hABC7). The **nucleotide** sequence was highly homologous to the ATM1 gene in yeast, which encodes an ABC **transporter** (yAtm1p) located in the **mitochondrial** inner

membrane. The deduced human product, a putative half-type **transporter**, consists of 752 amino acids that are 48.9% identical to those of yAtm[redacted] A computer-assisted protein s[redacted]ctural and localization analysis revealed that the **mitochondrial** targeting **signal** of yAtm1p is conserved in the N-terminal region of the primary sequence of the hABC7 protein, and therefore this product is also likely to be located in the **mitochondrial** inner membrane. The evidence strongly suggests that the hABC7 gene is a counterpart of ATM1 and that its product is probably involved in heme **transport**. We mapped the hABC7 gene to chromosome Xq13.1-q13.3 by fluorescence in-situ hybridization. As band Xq13 has been implicated in X-**linked** sideroblastic anemia with spinocerebellar ataxia, hABC7 becomes a candidate gene for this heritable disorder.

L14 ANSWER 3 OF 29 MEDLINE
ACCESSION NUMBER: 97087500 MEDLINE
DOCUMENT NUMBER: 97087500
TITLE: Regulation of endoplasmic reticulum-Ca-ATPase by glycolysis
in eukaryotic cells.
AUTHOR: Martinez-Zaguilan R; Wesson D E
CORPORATE SOURCE: Department of Physiology, Texas Tech University Health Sciences Center, Lubbock 79430, USA.
SOURCE: MINERAL AND ELECTROLYTE METABOLISM, (1996) 22 (5-6) 318-35.
Ref: 157
Journal code: M9Z. ISSN: 0378-0392.
PUB. COUNTRY: Switzerland
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199705
ENTRY WEEK: 19970503
AB This paper reviews work by our and other laboratories that explores the coupling between glycolysis and endoplasmic reticulum (ER)-Ca-ATPases in regulating Ca2+ homeostasis in several cell types. Changes in intracellular Ca2+ [(Ca2+]in) **link** interaction between hormones and cell surface receptors with the initiation of specific cellular functions. Thus, changes in [Ca2+]in mediate **signal** transduction mechanisms that modulate many physiological functions including cell growth, muscle cell contractility, and exocytosis in secretory cells. In most eukaryotic cells, total cellular Ca2+ is in the millimolar range, yet
only a fraction (i.e., nanomolar) is free in the cytosol. Cells use both active and 'passive' mechanisms to maintain [Ca2+]in within a narrow range. Active mechanisms include plasma membrane and endoplasmic/sarcoplasmic reticulum (ER/SR)-Ca-ATPases, Ca2+ channels (inositol trisphosphate- and voltage-sensitive), and Na+/Ca2+ exchangers. 'Passive' mechanisms include Ca(2+)-binding proteins (e.g., calsequestrin,
calmodulin, calreticulin). The relative contribution of active and 'passive' mechanisms to [Ca2+]in homeostasis in a given cell is not known.
Ca2+ might move among several intracellular compartments, including the ER/SR, **mitochondria**, **nucleus**, Golgi apparatus, endosomes and lysosomes. The ubiquitous distribution of ER-Ca-ATPases in these intracellular organelles suggests a major role of this pump in Ca2+ homeostasis, but the importance of intracellular compartments to [Ca2+]in homeostasis is not well understood. Glucose has been suggested to have a role in regulating some of these ion **transport** processes. Thus, the increased cell metabolism that follows glucose stimulation is associated with altered [Ca2+]in homeostasis. The precise mechanisms by which glucose or its metabolites modulate [Ca2+]in homeostasis are unknown

but might involve regulation of ER-Ca-ATPases.

L14 ANSWER 4 OF 29 MEDLINE
ACCESSION NUMBER: 96295547 MEDLINE
DOCUMENT NUMBER: 96295547
TITLE: Two components of the chloroplast protein import apparatus, IAP86 and IAP75, interact with the transit sequence during the recognition and translocation of precursor proteins at the outer envelope.
AUTHOR: Ma Y; Kouranov A; LaSala S E; Schnell D J
CORPORATE SOURCE: Department of Biological Sciences, Rutgers, State University of New Jersey, Newark 07102, USA.
SOURCE: JOURNAL OF CELL BIOLOGY, (1996 Jul) 134 (2) 315-27. Journal code: HMV. ISSN: 0021-9525.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199611
AB The interactions of precursor proteins with components of the **chloroplast** envelope were investigated during the early stages of protein import using a chemical cross-**linking** strategy. In the absence of energy, two components of the outer envelope import machinery, IAP86 and IAP75, cross-**linked** to the transit sequence of the precursor to the small subunit of ribulose-1, 5-bisphosphate carboxylase (pS) in a precursor binding assay. In the presence of concentrations of ATP or GTP that support maximal precursor binding to the envelope, cross-**linking** to the transit sequence occurred predominantly with IAP75 and a previously unidentified 21-kD polypeptide of the inner membrane, indicating that the transit sequence had inserted across the outer membrane. Cross-**linking** of envelope components to sequences in the mature portion of a second precursor, preferredoxin, was detected in the presence of ATP or GTP, suggesting that sequences distant from the transit sequence were brought into the vicinity of the outer membrane under these conditions. IAP75 and a third import component, IAP34, were coimmunoprecipitated with IAP86 antibodies from solubilized envelope membranes, indicating that these three proteins form a stable complex in the outer membrane. On the basis of these observations, we propose that IAP86 and IAP75 act as components of a multisubunit complex to mediate energy-independent recognition of the transit sequence and subsequent **nucleoside** triphosphate-induced insertion of the transit sequence across the outer membrane.

L14 ANSWER 5 OF 29 MEDLINE
ACCESSION NUMBER: 96144460 MEDLINE
DOCUMENT NUMBER: 96144460
TITLE: Mitochondria and diabetes. Genetic, biochemical, and clinical implications of the cellular energy circuit.
AUTHOR: Gerbitz K D; Gempel K; Brdiczka D
CORPORATE SOURCE: Institute of Clinical Chemistry, Academic Hospital Schwabing, Munchen, Germany.
SOURCE: DIABETES, (1996 Feb) 45 (2) 113-26. Ref: 152 Journal code: E8X. ISSN: 0012-1797.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199604
AB Physiologically, a postprandial glucose rise induces metabolic **signal** sequences that use several steps in common in both the pancreas and peripheral tissues but result in different events due to specialized tissue functions. Glucose **transport** performed by tissue-specific glucose **transporters** is, in general, not rate

limiting. The next step is phosphorylation of glucose by cell-specific hexokinases. In the beta-cell, glucokinase (or hexokinase IV) is activated upon binding to a pore protein in the outer **mitochondrial** membrane at contact sites between outer and inner membranes. The same mechanism applies for hexokinase II in skeletal muscle and adipose tissue. The activation of hexokinases depends on a contact site-specific structure of the pore, which is voltage-dependent and influenced by the electric potential of the inner **mitochondrial** membrane. **Mitochondria** lacking a membrane potential because of defects in the respiratory chain would thus not be able to increase the glucose-phosphorylating enzyme activity over basal state. Binding and activation of hexokinases to **mitochondrial** contact sites lead to an acceleration of the formation of both ADP and glucose-6-phosphate (G-6-P). ADP directly enters the **mitochondrion** and stimulates **mitochondrial** oxidative phosphorylation. G-6-P is an important intermediate of energy metabolism at the switch position between glycolysis, glycogen synthesis, and the pentose-phosphate shunt. Initiated by blood glucose elevation, **mitochondrial** oxidative phosphorylation is accelerated in a concerted action coupling glycolysis to **mitochondrial** metabolism at three different points: first, through NADH transfer to the respiratory chain complex I via the malate/aspartate shuttle; second, by providing FADH2 to complex II through the glycerol-phosphate/dihydroxy-acetone-phosphate cycle; and third, by the action of hexo(gluco)kinases providing ADP for complex V, the ATP synthetase. As cytosolic and **mitochondrial** isozymes of creatine kinase (CK) are observed in insulinoma cells, the phosphocreatine (CrP) shuttle, working in brain and muscle, may also be involved in signaling glucose-induced insulin secretion in beta-cells. An interplay between the plasma membrane-bound CK and the **mitochondrial** CK could provide a mechanism to increase ATP locally at the KATP channels, coordinated to the activity of **mitochondrial** CrP production. Closure of the KATP channels by ATP would lead to an increase of cytosolic and, even more, **mitochondrial** calcium and finally to insulin secretion. Thus in beta-cells, glucose, via bound glucokinase, stimulates **mitochondrial** CrP synthesis. The same signaling sequence is used in the opposite direction in muscle during exercise when high ATP turnover increases the creatine level that stimulates **mitochondrial** ATP synthesis and glucose phosphorylation via hexokinase. Furthermore, this cytosolic/**mitochondrial** cross-talk is also involved in activation of muscle glycogen synthesis by glucose. The activity of **mitochondrially** bound hexokinase provides G-6-P and stimulates UTP production through **mitochondrial nucleoside** diphosphate kinase. Pathophysiologically, there are at least two genetically different forms of diabetes **linked** to energy metabolism: the first example is one form of maturity-onset diabetes of the young (MODY2), an autosomal dominant disorder caused by point mutations of the glucokinase gene; the second example is several forms of **mitochondrial** diabetes caused by point and length mutations of the **mitochondrial** DNA (mtDNA) that encodes several subunits of the respiratory chain complexes. Because the mtDNA is vulnerable and accumulates point and length mutations during aging, it is likely to contribute to the manifestation of some forms of NIDDM.(ABSTRACT TRUNCATED)

L14 ANSWER 6 OF 29 MEDLINE
ACCESSION NUMBER: 94319107 MEDLINE
DOCUMENT NUMBER: 94319107
TITLE: Heinrich Wieland--prize lecture. **Transport** of proteins across mitochondrial membranes.
AUTHOR: Neupert W

CORPORATE SOURCE: Institut fur Physiologische Chemie, Physikalische Biochemie
u[redacted]Zellbiologie, Universitat Munc[redacted], Germany.
SOURCE: CLINICAL INVESTIGATOR, (1994 Mar) 72 (4) 251-61. Ref: 73
Journal code: BHE. ISSN: 0941-0198.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Biography
Historical
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199411

AB The vast majority of proteins comprising the **mitochondrion** are encoded by **nuclear** genes, synthesized on ribosomes in the cytosol, and translocated into the various **mitochondrial** subcompartments. During this process proteins must cross the lipid membranes of the **mitochondrion** without interfering with the integrity or functions of the organelle. In recent years an approach combining biochemical, molecular, genetic, and morphological methodology has provided insights into various aspects of this complex process of intracellular protein sorting. In particular, a greater understanding of the molecular specificity and mechanism of targeting of **mitochondrial** preproteins has been reached, as a protein complex of the outer membrane which facilitates recognition and initial membrane insertion has been identified and characterized. Furthermore, pathways and components involved in the translocation of pre-proteins across the two **mitochondrial** membranes are being dissected and defined. The energetics of translocation and the processes of unfolding and folding of proteins during transmembrane transfer are closely **linked** to the function of a host of proteins known as heat-shock proteins or molecular chaperones, present both outside and inside the **mitochondrion**. In addition, the analysis of the process of folding of polypeptides in the **mitochondrial** matrix has allowed novel and unexpected insights into general pathways of protein folding assisted by folding factors. Pathways of sorting of proteins to the four different **mitochondrial** subcompartments--the outer membrane (OM), intermembrane space, inner membrane (IM) and matrix--are only partly understood and reveal an amazing complexity and variation. Many additional protein factors are involved in these latter processes, a few of which have been analyzed, such as cytochrome c heme lyase and cytochrome c1 heme lyase, enzymes that catalyze the covalent addition of the heme group to cytochrome c and c1 preproteins, and the **mitochondrial** processing peptidase which cleaves **signal** sequences after import of preproteins into the matrix. Thus, the study of **transport** of polypeptides through the **mitochondrial** membranes does not only contribute to the understanding of how biological membranes facilitate the penetration of macromolecules but also provides novel insights into the structure and function of this organelle.

L14 ANSWER 7 OF 29 MEDLINE
ACCESSION NUMBER: 94207188 MEDLINE
DOCUMENT NUMBER: 94207188
TITLE: Truncated presequences of mitochondrial F1-ATPase beta subunit from Nicotiana plumbaginifolia **transport** CAT and GUS proteins into mitochondria of transgenic tobacco.
AUTHOR: Chaumont F; Silva Filho M de C; Thomas D; Leterme S; Boutry
M

CORPORATE SOURCE: Unite de Biochimie Physiologique, University of Louvain, Louvain-la-Neuve, Belgium.
SOURCE: PLANT MOLECULAR BIOLOGY, (1994 Feb) 24 (4) 631-41.
Journal code: A6O. ISSN: 0167-4412.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199407

AB The **mitochondrial** F1-ATPase beta subunit (ATPase-beta) of Nicotiana plumbaginifolia is **nucleus**-encoded as a precursor containing an NH2-terminal extension. By sequencing the mature N. tabacum ATPase-beta, we determined the length of the presequence, viz. 54 residues. To define the essential regions of this presequence, we produced a series of 3' deletions in the sequence coding for the 90 NH2-terminal residues of ATPase-beta. The truncated sequences were fused with the chloramphenicol acetyl transferase (cat) and beta-glucuronidase (gus) genes and introduced into tobacco plants. From the observed distribution of CAT and GUS activity in the plant cells, we conclude that the first 23 amino-acid residues of ATPase-beta remain capable of specifically targeting reporter proteins into **mitochondria**. Immunodetection in transgenic plants and in vitro import experiments with various CAT fusion proteins show that the precursors are processed at the expected cleavage site but also at a cryptic site located in the **linker** region between the presequence and the first methionine of native CAT.

L14 ANSWER 8 OF 29 MEDLINE
ACCESSION NUMBER: 94103193 MEDLINE
DOCUMENT NUMBER: 94103193
TITLE: Differential regulation of respiratory chain subunits by a CREB-dependent **signal** transduction pathway. Role of cyclic AMP in cytochrome c and COXIV gene expression.
AUTHOR: Gopalakrishnan L; Scarpulla R C
CORPORATE SOURCE: Department of Cell, Molecular, and Structural Biology, Northwestern University Medical School, Chicago, Illinois 60611.
CONTRACT NUMBER: GM32525-11 (NIGMS)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1994 Jan 7) 269 (1) 105-13.
Journal code: HIV. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199404

AB In vertebrate organisms, the molecular mechanisms by which extracellular signals regulate **mitochondrial** function and biogenesis are largely unknown. We have previously identified multiple cis-acting elements in both cytochrome c and cytochrome oxidase subunit IV (COXIV) genes that are likely targets for the regulated expression of respiratory chain components. We now demonstrate that cytochrome c but not COXIV mRNA is induced by cAMP through a mechanism involving transcriptional activation. Maximal induction occurs within 3 h and does not require de novo protein synthesis. The differential response of these genes is mediated by two distinct cAMP response elements (CREs) in the cytochrome c promoter region. Both elements function independently to drive cAMP-dependent expression from a heterologous promoter and within the proper cytochrome c promoter context. In addition, the binding properties of both elements to **nuclear** factors were characterized by competition DNase I footprinting, methylation interference footprinting, site-directed mutagenesis, and UV-induced DNA-protein cross-**linking**. The results are all consistent with the specific recognition of both CREs by CRE binding protein (CREB). A highly purified preparation of recombinant CREB formed a specific complex with each of the

cytochrome c CREs identical to that formed with a crude **nuclear** fraction. In addition, the trans-activation of cytochrome c gene expression by recombinant CREB and protein kinase A in transfected cells was completely dependent on functional CREs within the promoter. These results establish that respiratory chain gene expression can be regulated directly by cAMP through a CREB-dependent **signal** transduction pathway.

L14 ANSWER 9 OF 29 MEDLINE
ACCESSION NUMBER: 94075404 MEDLINE
DOCUMENT NUMBER: 94075404
TITLE: Retrograde lipid traffic in yeast: identification of two distinct pathways for internalization of fluorescent-labeled phosphatidylcholine from the plasma membrane.
AUTHOR: Kean L S; Fuller R S; Nichols J W
CORPORATE SOURCE: Department of Physiology, Emory University School of Medicine, Atlanta, Georgia 30322..
CONTRACT NUMBER: GM39697 (NIGMS)
SOURCE: JOURNAL OF CELL BIOLOGY, (1993 Dec) 123 (6 Pt 1) 1403-19.

Journal code: HMV. ISSN: 0021-9525.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199403
AB Digital, video-enhanced fluorescence microscopy and spectrofluorometry were used to follow the internalization into the yeast Saccharomyces cerevisiae of phosphatidylcholine molecules labeled on one acyl chain with the fluorescent probe 7-nitrobenz-2-oxa-1,3-diazol-4-yl (NBD). Two pathways were found: (1) **transport** by endocytosis to the vacuole and (2) **transport** by a non-endocytic pathway to the **nuclear** envelope and **mitochondria**. The endocytic pathway was inhibited at low temperature (< 2 degrees C) and by ATP depletion. Mutations in secretory (SEC) genes that are necessary for membrane traffic through the secretory pathway (including SEC1, SEC2, SEC4, SEC6, SEC7, SEC12, SEC14, SEC17, SEC18, and SEC21) almost completely blocked endocytic uptake. In contrast, mutations in the SEC63, SEC65, or SEC11 genes, required for translocation of nascent secretory polypeptides into the ER or **signal** peptide processing in the ER, only slightly reduced endocytic uptake. Phospholipid endocytosis was also independent of the gene encoding the clathrin heavy chain, CHC1. The correlation of biochemical analysis with fluorescence microscopy indicated that the fluorescent phosphatidylcholine was degraded in the vacuole and that degradation was, at least in part, dependent on the vacuolar proteolytic cascade. The non-endocytic route functioned with a lower cellular energy charge (ATP levels 80% reduced) and was largely independent of the SEC genes. Non-endocytic **transport** of NBD-phosphatidylcholine to the **nuclear** envelope and **mitochondria** was inhibited by pretreatment of cells with the sulfhydryl reagents N-ethylmaleimide and p-chloromercuribenzenesulfonic acid, suggesting the existence of protein-mediated transmembrane transfer (flip-flop) of phosphatidylcholine across the yeast plasma membrane. These data establish a **link** between lipid movement during secretion and endocytosis in yeast and suggest that phospholipids may also gain access to intracellular organelles through non-endocytic, protein-mediated events.

L14 ANSWER 10 OF 29 MEDLINE
ACCESSION NUMBER: 91177897 MEDLINE
DOCUMENT NUMBER: 91177897
TITLE: The MAS-encoded processing protease of yeast mitochondria.

Interaction of the purified enzyme with **signal** peptides and a purified precursor protein.
AUTHOR: Yaffe M J; Geli V; Oppliger W; Suda K; James P; Schatz G
CORPORATE SOURCE: Biocenter, University of Basel, Switzerland.
CONTRACT NUMBER: 2 R01 GM 37803 (NIGMS)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1991 Apr 5) 266 (10) 6416-23.
Journal code: HIV. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199107
AB The matrix of yeast **mitochondria** contains a chelator-sensitive protease that removes matrix-targeting signals from most precursor proteins **transported** into this compartment. The enzyme consists of two nonidentical subunits that are encoded by the **nuclear** genes MAS1 and MAS2. With the aid of these cloned genes, we have now overexpressed the active holoenzyme in yeast, purified it in milligram amounts, and studied its biochemical and physical properties. Atomic absorption analysis shows that the purified enzyme lacks significant amounts of zinc, manganese, or cobalt; if none of these metal ions is added during the assay, the enzyme is catalytically inactive but can still cleave substoichiometric amounts of substrate. The amino-terminal sequences of the two mature subunits were determined; comparison with the deduced amino acid sequences of the corresponding precursors revealed that the MAS1 and MAS2 subunits are synthesized with prepeptides composed of 19 and 13 residues, respectively, which have similar sequences. The enzyme is inhibited competitively by chemically synthesized matrix-targeting peptides; the degree of inhibition correlates with the peptides' targeting efficacy. Matrix-targeting peptides containing the cleavage site of the corresponding authentic precursor protein are cleaved correctly by the purified enzyme. A purified artificial precursor protein bound to the holoenzyme can be photocross-**linked** to the MAS2 subunit.

L14 ANSWER 11 OF 29 MEDLINE
ACCESSION NUMBER: 90199881 MEDLINE
DOCUMENT NUMBER: 90199881
TITLE: Facilitated nuclear **transport** of histone H1 and other small nucleophilic proteins.
AUTHOR: Breeuwer M; Goldfarb D S
CORPORATE SOURCE: Department of Biology, University of Rochester, New York 14627..
SOURCE: CELL, (1990 Mar 23) 60 (6) 999-1008.
Journal code: CQ4. ISSN: 0092-8674.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199007
AB Upon microinjection into the cytoplasm, three small nonnuclear (extracellular or **mitochondrial**) proteins diffused into **nuclei** of chilled or energy-depleted cells. In contrast, the facilitated **transport** of two large **nuclear** localization **signal** (NLS)-containing proteins was reversibly arrested by chilling or energy depletion. Surprisingly, the **transport** of two small **nucleophilic** proteins, histone H1 and P(Lys)-cytochrome c (cytochrome c cross-**linked** with synthetic peptide NLSs), was also arrested by either chilling or energy depletion. In situ titration studies indicate that the **transport** arrest of H1 in chilled cells is mediated by a cytoplasmic receptor.

Therefore, even though they are potentially able to diffuse into **nuclei**, histones and other small NLS-containing proteins are localized by a receptor-mediated process that precludes their diffusion through the **nuclear** pores.

L14 ANSWER 12 OF 29 MEDLINE
ACCESSION NUMBER: 90130693 MEDLINE
DOCUMENT NUMBER: 90130693
TITLE: Import of proteins into the chloroplast lumen.
AUTHOR: Weisbeek P; Hageman J; de Boer D; Pilon R; Smeekens S
CORPORATE SOURCE: Department of Molecular Cell Biology, University of Utrecht, The Netherlands..
SOURCE: JOURNAL OF CELL SCIENCE. SUPPLEMENT, (1989) 11 199-223. Ref: 44
Journal code: HNG. ISSN: 0269-3518.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199005

AB Plastocyanin is a **nuclear**-encoded protein that is functional in the thylakoid lumen of the **chloroplast**. It is synthesized in the cytoplasm as a precursor with an N-terminal transit peptide of 66 amino acids. Its **transport** route involves two steps, import into the **chloroplasts** and subsequent routing over the thylakoid membrane into the lumen. Concomitant with the **transport**, the transit peptide is removed in two successive steps. The transit peptide consists of two functionally different domains. In this study we examine to what extent each domain is involved in import and routing and how far these two processes are **linked**. For this purpose we made deletions in the N-terminal and C-terminal part of the transit peptide and fusion proteins which only contain one of these parts. The results show that the N-terminal part of the transit peptide is responsible for import into the **chloroplast**. The N-terminal 43 amino acids are sufficient to direct other proteins into the stroma. The C-terminal part of the transit peptide is a prerequisite for routing inside the **chloroplast** but not for import. When deletions are made in this part, the **transport** of plastocyanin stops after import and the intermediate accumulates in the stroma or on the outside of the thylakoids. Transgenic tomato plants that constitutively express a foreign plastocyanin gene were used to study protein **transport** in different tissues. Normally, expression of endogenous plastocyanin genes in plants is restricted to photosynthetic tissues only. However, in the transgenic plants this foreign plastocyanin protein is found in all tissues examined. The protein is **transported** into the local plastids of these tissues and it is processed to the mature size. We conclude that plastids of developmentally different tissues are capable of importing precursor proteins that are normally not found in these tissues. Most likely such plastids, though functionally and morphologically differentiated, have similar or identical protein import mechanisms when compared to the **chloroplasts** in green tissue. The precursor of ferredoxin was expressed in Escherichia coli. Surprisingly the precursor interacts with the cytoplasmic membrane and is translocated across this membrane. The unprocessed precursor accumulates in the periplasm.

L14 ANSWER 13 OF 29 MEDLINE
ACCESSION NUMBER: 89255504 MEDLINE
DOCUMENT NUMBER: 89255504
TITLE: Biogenesis of cytochrome c1. Role of cytochrome c1 heme lyase and of the two proteolytic processing steps during import into mitochondria.

AUTHOR: Nicholson D W; Stuart R A; Neupert W
CORPORATE SOURCE: Institut fur Physiologische Chemie der Universitat Munchen, Federal Republic of Germany.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1989 Jun 15) 264 (17) 10156-68.
Journal code: HIV. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198909

AB The biogenesis of cytochrome c1 involves a number of steps including: synthesis as a precursor with a bipartite **signal** sequence, transfer across the outer and inner **mitochondrial** membranes, removal of the first part of the presequence in the matrix, reexport to the outer surface of the inner membrane, covalent addition of heme, and removal of the remainder of the presequence. In this report we have focused on the steps of heme addition, catalyzed by cytochrome c1 heme lyase, and of proteolytic processing during cytochrome c1 import into **mitochondria**. Following translocation from the matrix side to the intermembrane-space side of the inner membrane, apocytochrome c1 forms a complex with cytochrome c1 heme lyase, and then holocytochrome c1 formation occurs. Holocytochrome c1 formation can also be observed in detergent-solubilized preparations of **mitochondria**, but only after apocytochrome c1 has first interacted with cytochrome c1 heme lyase to produce this complex. Heme **linkage** takes place on the intermembrane-space side of the inner **mitochondrial** membrane and is dependent on NADH plus a cytosolic cofactor that can be replaced by flavin **nucleotides**. NADH and FMN appear to be necessary for reduction of heme prior to its **linkage** to apocytochrome c1. The second proteolytic processing of cytochrome c1 does not take place unless the covalent **linkage** of heme to apocytochrome c1 precedes it. On the other hand, the cytochrome c1 heme lyase reaction itself does not require that processing of the cytochrome c1 precursor to intermediate size cytochrome c1 takes place first. In conclusion, cytochrome c1 heme lyase catalyzes an essential step in the import pathway of cytochrome c1, but it is not involved in the transmembrane movement of the precursor polypeptide. This is in contrast to the case for cytochrome c in which heme addition is coupled to its **transport** directly across the outer membrane into the intermembrane space.

L14 ANSWER 14 OF 29 MEDLINE
ACCESSION NUMBER: 89066793 MEDLINE
DOCUMENT NUMBER: 89066793
TITLE: Complete kinetic and thermodynamic characterization of the unisite catalytic pathway of Escherichia coli F1-ATPase. Comparison with mitochondrial F1-ATPase and application to the study of mutant enzymes.
AUTHOR: Al-Shawi M K; Senior A E
CORPORATE SOURCE: Department of Biochemistry, University of Rochester Medical Center, New York 14642.
CONTRACT NUMBER: GM25349 (NIGMS)
GM29805 (NIGMS)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1988 Dec 25) 263 (36) 19640-8.
Journal code: HIV. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198903

AB A complete analysis is presented of the component rate constants of the "unisite" reaction pathway in normal Escherichia coli F1-ATPase. Gibbs free energy profiles of the unisite reaction pathway were constructed for

both normal E. coli F1 and bovine-heart **mitochondrial** F1, and comparison indicated that E. coli F1 is an ancestral form of the **mitochondrial** enzyme. Similar kinetic and thermodynamic analyses of the unisite reaction pathway were done for mutant beta-Asn-242 and beta-Val-242 E. coli F1-ATPases. Both mutations affected unisite binding and hydrolysis of MgATP but had little effect on release of products or binding of MgADP. It was apparent that a primary effect of the mutations was on the interaction between the catalytic **nucleotide**-binding domain and the substrate MgATP. The catalytic transition state [F1-ATP]++ was the most destabilized step in the reaction sequence. Measurements of delta delta G[F1.ATP]++ and linear free energy plots for the catalytic step were consistent with the view that, in normal enzyme, residue beta-Asp-242 accepts an H-bond from the transition-state substrate in order to facilitate catalysis. Both mutations impaired positive catalytic cooperativity. This was caused by energetic destabilization of the catalytic transition state and was an indirect effect, not a direct effect on **signal** transmission per se between catalytic **nucleotide**-binding domains on beta-subunits. Therefore, impairment of unisite catalysis and of positive catalytic cooperativity appeared to be **linked**. This may provide a unifying explanation as to why a series of other, widely separated mis-sense mutations within the catalytic **nucleotide**-binding domain on F1-beta-subunit, which have been reported to affect unisite catalysis, also impair positive catalytic cooperativity. Linear free energy plots for the ATP-binding step of unisite catalysis demonstrated that beta-Asn-242 and beta-Val-242 mutant enzymes did not suffer any gross disruptive change in structure of the catalytic **nucleotide**-binding domain, reinforcing the view that impairment of catalysis was due to a localized effect. Such analyses confirmed that six other F1-beta-subunit mutants, previously generated and characterized in this laboratory and thought to have inhibitory side-chain substitutions in the catalytic **nucleotide**-binding domain, are also devoid of gross structural disruption.

L14 ANSWER 15 OF 29 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1994:251530 BIOSIS
DOCUMENT NUMBER: PREV199497264530
TITLE: **Transport** of proteins across mitochondrial membranes.
AUTHOR(S): Neupert, W.
CORPORATE SOURCE: Inst. Physiol. Chemie, Physikalische Biochemie Zellbiol., Univ. Muenchen, D-80336 Muenchen Germany
SOURCE: Clinical Investigator, (1994) Vol. 72, No. 4, pp. 251-261.
ISSN: 0941-0198.
DOCUMENT TYPE: General Review
LANGUAGE: English

AB The vast majority of proteins comprising the **mitochondrion** are encoded by **nuclear** genes, synthesized on ribosomes in the cytosol, and translocated into the various **mitochondrial** subcompartments. During this process proteins must cross the lipid membranes of the **mitochondrion** without interfering with the integrity or functions of the organelle. In recent years an approach combining biochemical, molecular, genetic, and morphological methodology has provided insights into various aspects of this complex process of intracellular protein sorting. In particular, a greater understanding of the molecular specificity and mechanism of targeting of **mitochondrial** preproteins has been reached, as a protein complex of the outer membrane which facilitates recognition and initial membrane insertion has been identified and characterized. Furthermore, pathways and components involved in the translocation of preproteins across the two **mitochondrial** membranes are being dissected and defined. The

energetics of translocation and the processes of unfolding and folding of proteins during transmembrane transfer are closely linked to the function of a host of proteins known as heat-shock proteins or molecular chaperones, present both outside and inside the **mitochondrion**. In addition, the analysis of the process of folding of polypeptides in the **mitochondrial** matrix has allowed novel and unexpected insights into general pathways of protein folding assisted by folding factors. Pathways of sorting of proteins to the four different **mitochondrial** subcompartments - the outer membrane (OM), intermembrane space, inner membrane (IM) and matrix - are only partly understood and reveal an amazing complexity and variation. Many additional protein factors are involved in these latter processes, a few of which have been analyzed, such as cytochrome c heme lyase and cytochrome c-1 heme lyase, enzymes that catalyze the covalent addition of the heme group to cytochrome c and c-1 preproteins, and the **mitochondrial** processing peptidase which cleaves **signal** sequences after import of preproteins into the matrix. Thus, the study of **transport** of polypeptides through the **mitochondrial** membranes does not only contribute to the understanding of how biological membranes facilitate the penetration of macromolecules but also provides novel insights into the structure and function of this organelle.

L14 ANSWER 16 OF 29 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:278118 CAPLUS
DOCUMENT NUMBER: 132:304288
TITLE: Regulation of transcription or intracellular signaling using fusion proteins containing conditional aggregation domains (CAD)
INVENTOR(S): Clackson, Timothy; Rivera, Victor
PATENT ASSIGNEE(S): Ariad Gene Therapeutics, Inc., USA
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000023600	A1	20000427	WO 1999-US24328	19991019

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1998-174767 19981019
US 1998-PV104752 19981019

AB A system for regulation of transcription or intracellular signaling is developed by using fusion proteins contg. conditional aggregation domains (CAD). The fusion proteins contg. transcription regulation domain, or DNA binding domain, or cellular localization **signal** or domain, or cellular signaling domain etc. in addn. to one or more CAD (such as FKBP domain or its mutant F36M or W59V) aggregate with one another in the absence of the ligands (rapamycin or its analog AP22542, AP21998, FK506 etc.), and these aggregated complex disperse following the exposure of the ligands. For transcription regulation, one or two CAD-fusion protein(s) contg. a transcription activation or repression domain (TAD or TRD) and/or

a DNA binding domain (DB) , is/are introduced to cells with a target gene operably **linked** to [redacted] sequence recognized by DB. For [redacted] cellular signaling, one or [redacted] CAD-fusion protein(s) contg. [redacted] membrane-targeting domain and/or a cellular signaling domain (such as the cytoplasmic domain of a receptor for a growth factor or cytokine), is/are introduced to target cells. These fusion protein are designed to localize at the cell membrane by itself or by being recruited through the other fusion protein to aggregate/disaggregate and induce/block the cellular **signal** upon the addn. of ligands. The system is exemplified by transfecting HT1080 cells with vectors expressing a fusion protein of F36M or W59V FKBP with a DB ZFHD1 and a TAD NF-.kappa.B p65 subunit for controlling the switch-on or switch-off of the transcription of the reporter gene driven by ZFHD1 binding site. In addn., the invention provides methods for identifying novel CADs using yeast two hybrid system. This method may be applied for ligand-dependent regulation of many biol. events.

REFERENCE COUNT: 4

REFERENCE(S):
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(4) Univ Leland Stanford Junior; WO 9418317 A 1994

L14 ANSWER 17 OF 29 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 2000:93338 CAPLUS
DOCUMENT NUMBER: 132:235286

TITLE: Roles of mitochondrial ATP-sensitive K channels and PKC in anti-infarct tolerance afforded by adenosine A1 receptor activation

AUTHOR(S): Miura, Tetsuji; Liu, Yongge; Kita, Hiroyuki; Ogawa, Takashi; Shimamoto, Kazuaki
CORPORATE SOURCE: Second Department of Internal Medicine, Sapporo Medical University School of Medicine, Sapporo, Japan

SOURCE: J. Am. Coll. Cardiol. (2000), 35(1), 238-245
CODEN: JACCDI; ISSN: 0735-1097
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB This study intended to assess the role of mitochondrial ATP-sensitive potassium (mitoKATP) channels and the sequence of **signal** transduction with protein kinase C (PKC) and adenosine A1 receptors in rabbits. To our knowledge, the **link** between trigger receptors of preconditioning, PKC and mitoKATP channels has not been examd. in a whole heart model of infarction. In the first series of expts., myocardial infarction was induced in isolated buffer-perfused rabbit hearts by 30-min global ischemia and 2-h reperfusion. Infarct size in the left ventricle was detd. by tetrazolium staining and expressed as a percentage of area at risk (i.e., the whole left ventricle) (%IS/AR). In the second series of expts., mitochondria were isolated from the heart, and their respiratory function was examd. using glutamate as a substrate. Pretreatment with R-phenylisopropyladenosine (R-PIA, 1 .mu.mol/L), an A1-receptor agonist, reduced %IS/AR from 49.8 .+-. 6.5% to 13.4 .+-. 2.9%. This protection was abolished by calphostin C, a PKC inhibitor, and by 5-hydroxydecanoate (5-HD), a selective inhibitor of mitoKATP channels. A selective mitoKATP channel opener, diazoxide (100 .mu.mol/L), mimicked the effect of R-PIA on infarct size (%IS/AR = 11.6 .+-. 4.0%), and this protective effect was also abolished by 5-HD. However, calphostin C failed to block the infarct size-limiting effect of diazoxide. Neither calphostin C nor 5-HD alone modified %IS/AR. State III respiration (Qo2) and respiratory control index (RCI) were reduced after 30 min of ischemia (Qo2 = 147.3 .+-. 5.3 vs. 108.5 .+-. 12.3, RCI = 22.3 .+-. 1.1 vs. 12.1 .+-. 1.8, $p < 0.05$). This mitochondrial dysfunction was persistent after 10 min of reperfusion (Qo2 = 96.1 .+-. 15.5, RCI = 9.5 .+-. 1.9).

Diazoxide significantly attenuated the respiratory dysfunction after 30 min of ischemia (Qo2 = 142.8 .+-. 9.7, RCI = 16.2 . 0.8) and subsequent 10-min reperfusion (Qo2 = 135.3 .+-. 7.2, RCI = 19.1 .+-. 0.8). These results suggest that mitoKATP channels are downstream of PKC in the mechanism of infarct-size limitation by A1-receptor activation and that the anti-infarct tolerance afforded by opening of mitoKATP channels is assocd. with preservation of mitochondrial function during ischemia/reperfusion.

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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 18 OF 29 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:767840 CAPLUS
DOCUMENT NUMBER: 132:62266
TITLE: Apoptosis driven by IP3-**linked** mitochondrial calcium signals
AUTHOR(S): Szalai, Gabor; Krishnamurthy, Rajeshwari; Hajnoczky, Gyorgy
CORPORATE SOURCE: Department of Pathology, Anatomy and Cell Biology, Thomas Jefferson University, Philadelphia, PA, 19107, USA
SOURCE: EMBO J. (1999), 18(22), 6349-6361
CODEN: EMJODG; ISSN: 0261-4189
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Increases of mitochondrial matrix [Ca2+] ([Ca2+]m) evoked by calcium mobilizing agonists play a fundamental role in the physiol. control of cellular energy metab. Here, we report that apoptotic stimuli induce a switch in mitochondrial calcium signaling at the beginning of the apoptotic process by facilitating Ca2+-induced opening of the mitochondrial permeability transition pore (PTP). Thus [Ca2+]m signals evoked by addn. of large Ca2+ pulses or, unexpectedly, by IP3-mediated cytosolic [Ca2+] spikes trigger mitochondrial permeability transition and, in turn, cytochrome c release. IP3-induced opening of PTP is dependent on a privileged Ca2+ **signal** transmission from IP3 receptors to mitochondria. After the decay of Ca2+ spikes, resealing of PTP occurs allowing mitochondrial metab. to recover, whereas activation of caspases is triggered by cytochrome c released to the cytosol. This organization provides an efficient mechanism to establish caspase activation, while mitochondrial metab. is maintained to meet ATP requirements of apoptotic cell death.

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REFERENCE(S):
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 19 OF 29 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:524467 CAPLUS
DOCUMENT NUMBER: 131:269381
TITLE: A multisubunit complex of outer and inner mitochondrial membrane protein translocases stabilized

in vivo by translocation intermediates
AUTHOR(S): [redacted]Schulke, Norbert; Sepuri, Nares[redacted]Babu V.; Gordon, Donna M.; Saxena, Sandeep; Dan[redacted], Andrew; Pain, Debkumar
CORPORATE SOURCE: Department of Physiology, University of Pennsylvania School of Medicine, Philadelphia, PA, 19104-6085, USA
SOURCE: J. Biol. Chem. (1999), 274(32), 22847-22854
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Translocation of **nuclear** encoded preproteins into the **mitochondrial** matrix requires the coordinated action of two translocases: one (Tom) located in the outer **mitochondrial** membrane and the other (Tim) located in the inner membrane. These translocases reversibly cooperate during protein import. We have previously constructed a chimeric precursor (pPGPrA) consisting of an authentic **mitochondrial** precursor at the N terminus (.DELTA.1-pyrroline-5-carboxylate dehydrogenase, pPut) **linked**, through glutathione S-transferase, to protein A. When pPGPrA is expressed in yeast, it becomes irreversibly arrested during translocation across the outer and inner **mitochondrial** membranes. Consequently, the two membranes of **mitochondria** become progressively "zippered" together, forming long stretches in which they are in close contact. We now demonstrate that trapped PGPrA intermediates hold the import channels stably together and inhibit **mitochondrial** protein import and cell growth. Using IgG-Sepharose affinity chromatog. of solubilized zippered membranes, we have isolated a multisubunit complex that contains all Tom and Tim components known to be essential for import of matrix-targeted proteins, namely Tom40, Tom22, Tim17, Tim23, Tim44, and matrix-localized Hsp70. Further characterization of this complex may shed light on structural features of the complete **mitochondrial** import machinery.
REFERENCE COUNT: 46
REFERENCE(S): (1) Arnold, I; FEBS Lett 1997, V411, P195 CAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 20 OF 29 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:476517 CAPLUS
DOCUMENT NUMBER: 131:227018
TITLE: Mitochondrial protein and HSP70 signaling after ischemia in hypothermic-adapted hearts augmented with glucose
AUTHOR(S): Ning, Xue-Han; Xu, Cheng-Su; Portman, Michael A.
CORPORATE SOURCE: Cardiology Division, Department of Pediatrics, University of Washington, Seattle, WA, 98195, USA
SOURCE: Am. J. Physiol. (1999), 277(1, Pt. 2), R11-R17
CODEN: AJPHAP; ISSN: 0002-9513
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Hypothermia improves resistance to subsequent ischemia in the cardioplegic-arrested heart (CAH). This adaptive process produces mRNA elevation for heat-shock protein (HSP) 70-1 and **mitochondrial** proteins, adenine **nucleotide** translocator (ANT1), and .beta.-F1-ATPase. Glucose in cardioplegia also enhances myocardial protection. These processes might be **linked** to reduced ATP depletion. To assess for synergism between these protective processes,

isolated rabbit hearts were perfused at 37.degree. and exposed to ischemic cardioplegic arre for 2 h. Hearts were in four groups: control (C), hypothermia adapted (H) perfused to 31.degree. 20 min before ischemia, 22 mM glucose (G) in cardioplegia, and hypothermic adaptation and glucose (HG). Developed pressure (DP), dP/dtmax, and pressure-rate product (PRP) improved in G, H, and HG compared with C during reperfusion. DP and PRP were elevated in HG over H and G. ATP was higher in G, H, and HG, although no addnl. increase in HG over H was found. Lactate and CO2 prodn. were elevated in G only. The mRNA expression for HSP70-1, ANT1, and .beta.-F1-ATPase was elevated severalfold in H and HG, but not G over C during reperfusion. In conclusion, glucose provides addnl. functional improvement in H. Addnl., neither ATP levels nor anaerobic metab. are **linked** to mRNA expression for HSP70, ANT1, or .beta.-F1-ATPase in CAH.

REFERENCE COUNT: 25
REFERENCE(S): (1) Benjamin, I; J Clin Invest 1992, V89, P1685 CAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 21 OF 29 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1999:71500 CAPLUS
DOCUMENT NUMBER: 130:248481

TITLE: Identification and characterization of a mammalian mitochondrial ATP-binding cassette membrane protein

AUTHOR(S): Hogue, Douglas L.; Liu, Lin; Ling, Victor
CORPORATE SOURCE: BC Cancer Research Centre, Vancouver, BC, V5Z 4L3, Can.

SOURCE: J. Mol. Biol. (1999), 285(1), 379-389
CODEN: JMOBAK; ISSN: 0022-2836
PUBLISHER: Academic Press
DOCUMENT TYPE: *Journal*
LANGUAGE: English

AB Membrane proteins of the ATP-binding cassette (ABC) superfamily are involved in the **transport** of diverse substrates across organellar and plasma membranes of the mammalian cell. Most human ABC proteins identified to date are assocd. with genetically **linked** diseases or clin. relevant phenotypes. We describe a new human half-mol. ABC protein, designated M-ABC1, that contains a predicted single membrane and ATP-binding cassette domain. M-ABC1 is localized to membranes of the mitochondria and its transcript is expressed in all tissues. The N-terminal region of the M-ABC1 protein was shown to function independently as a mitochondrial **signal** sequence by its ability to target the green fluorescent protein to the mitochondria. The monomeric 60 kDa M-ABC1 protein was chem. crosslinked in vivo into a major protein species of 120-130 kDa, thereby confirming that M-ABC1 exists within a higher ordered ABC protein complex. A dominant neg. repression approach using M-ABC1 protein with site-directed mutations in its Walker A motif revealed that the mutant protein was rapidly degraded and indicated that the intact Walker A motif of M-ABC1 was required for its stability. The identification of M-ABC1 extends the known distribution of members of the ABC protein family into the mammalian mitochondrion. (c) 1999 Academic Press.

REFERENCE COUNT: 51
REFERENCE(S): (1) Allikmets, R; Hum Mol Genet 1996, V5, P1649 CAPLUS
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ALL CITATIONS AVAILABLE IN THE [redacted] FORMAT

L14 ANSWER 22 OF 29 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1995:452111 CAPLUS
DOCUMENT NUMBER: 122:232688
TITLE: Small **nuclear**-encoded RNAs that are **transported** into mammalian **mitochondria** and their potential therapeutic uses
INVENTOR(S): Williams, R. Sanders; Li, Kang
PATENT ASSIGNEE(S): Board of Reagents, University of Texas System, USA
SOURCE: PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9429445	A1	19941222	WO 1994-US6132	19940601
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KG, KP, KR, KZ, LK, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, TJ, TT, UA, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5569754	A	19961029	US 1993-76094	19930611
AU 9469619	A1	19950103	AU 1994-69619	19940601
PRIORITY APPLN. INFO.:			US 1993-76094	19930611
			WO 1994-US6132	19940601

AB Small **nuclear**-encoded RNAs of mammalian cells that are specifically imported into **mitochondria** are described. The RNAs are from genes transcribed by polIII and bind to several **nucleolar** peptides and thus provide potential carriers for import of biol. mols., including metabolites and proteins, into the **mitochondrial** compartment. **Mitochondrial** dysfunction in several maternally inherited human diseases may be correctable employing **linkage** of **mitochondrial** import **signal** to **mitochondrial** tRNA sequences expressed from **nuclear** trans-genes without requirement for direct genetic transformation of **mitochondria**. Mutational anal. of the gene for the RNA of the **mitochondrial** RNA processing endonuclease (MRP) indicated that one of the mutants disappeared from the cellular pool at an unexpectedly high rate. This was found to be due to partitioning of the transcript into the **mitochondria**. Further studies showed that transcript was found in **nucleoli** and **mitochondria** and that transcription of the gene was coordinated with levels of **mitochondrial** biogenesis.

L14 ANSWER 23 OF 29 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1994:530875 CAPLUS
DOCUMENT NUMBER: 121:130875
TITLE: Mitochondrial Ca2+ homeostasis in intact cells
AUTHOR(S): Rizzuto, Rosario; Bastianutto, Carlo; Brini, Marisa; Murgia, Marta; Pozzan, Tullio
CORPORATE SOURCE: Dep. Biomedical Sci., Univ. Padova, Padua, 35121, Italy
SOURCE: J. Cell Biol. (1994), 126(5), 1183-94
CODEN: JCLBA3; ISSN: 0021-9525
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Ca2+ is a key regulator not only of multiple cytosolic enzymes, but also of a variety of metabolic pathways occurring within the lumen of intracellular organelles. Until recently, no technique to selectively monitor the Ca2+ concn. within defined cellular compartments was

available. The authors have recently proposed the use of molecularly engineered Ca2+-sensitive photoproteins to obtain such a result and demonstrated the application of this methodol. to the study of **mitochondrial** and **nuclear** Ca2+ dynamics. The authors here describe in more detail the use of chimeric recombinant aequorin targeted to the **mitochondria**. The technique can be applied with equiv. results to different cell models, transiently or permanently transfected. In all the cell types the authors analyzed, **mitochondrial** Ca2+ concn. ([Ca2+]m) increases rapidly and transiently upon stimulation with agonists coupled to inositol trisphosphate (InsP3) generation. The authors confirm that the high speed of **mitochondrial** Ca2+ accumulation with this type of stimuli depends on the generation of local gradients of Ca2+ in the cytosol, close to the channels sensitive to InsP3. In fact, only activation of these channels, but not the simple release from internal stores, as that elicited by blocking the intracellular Ca2+ ATPases, results in a fast **mitochondrial** Ca2+ accumulation. The authors also provide evidence in favor of a microheterogeneity among **mitochondria** of the same cells, about 30% of them apparently sensing the microdomains of high cytosolic Ca2+ concn. ([Ca2+]c). The changes in [Ca2+]m appear sufficiently large to induce a rapid activation of **mitochondrial** dehydrogenases, which can be followed by monitoring the level of NAD(P)H fluorescence. A general scheme can thus be envisaged by which the triggering of a plasma membrane receptor coupled to InsP3 generation raises the Ca2+ concn. both in the cytoplasm (thereby triggering energy-consuming processes, such as cell proliferation, motility, secretion, etc.) and in the **mitochondria**, where it activates the metabolic activity according to the increased cell needs.

L14 ANSWER 24 OF 29 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1993:404683 CAPLUS
DOCUMENT NUMBER: 119:4683
TITLE: Selective import of **nuclear**-encoded tRNAs into **mitochondria** of the protozoan Leishmania tarentolae
AUTHOR(S): Lye, Lon F.; Chen, Dwun Hou Tom; Suyama, Yoshitaka
CORPORATE SOURCE: Dep. Biol., Univ. Pennsylvania, Philadelphia, PA, 19104, USA
SOURCE: Mol. Biochem. Parasitol. (1993), 58(2), 233-45
CODEN: MBIPDP; ISSN: 0166-6851
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The trypanosomatid **mitochondrial** genome does not encode tRNA genes at all and exptl. evidence obtained with Leishmania tarentolae shows that tRNAs in **mitochondria** represent a selected set of imported **nuclear**-encoded tRNAs. In this paper, data are presented showing that tRNAs derived from the clustered genomic tRNA genes are invariably imported into **mitochondria**, while tRNA from the solitary gene is not. By sequencing a cosmid DNA clone of L. tarentolae genomic DNA, the authors identified a 1.5-kb subclone encoding a duplicate set of the closely **linked** tRNATyr (GTA) and tRNAThr (AGT) genes. Northern anal. shows that these tRNAs are imported into **mitochondria**. In contrast, when the tRNA gene [tRNAGln(CUG)] located alone in a 40-kb DNA fragment was examd., the corresponding tRNA was not detected in the **mitochondrion**. This "loner" tRNA gene is highly unusual since the 3'-flanking putative RNA polymerase III transcription termination **signal** sequence is characterized by a long string of 8 Ts followed by an A and a stretch of 7 Cs, while all other trypanosomatid tRNA genes whose tRNA transcripts are imported are terminated by a possible transcription termination **signal** of only 4-6 Ts. Whether the correlation found between the gene organization and tRNA-import characteristics is of general significance needs to be investigated further. A simple computer anal. presented in this paper rules out the

possibility that tRNAs found in the trypanosomatid **mitochondrion** are the products the U-addn. type RNA editing of maxicircle DNA.

L14 ANSWER 25 OF 29 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1991:579579 CAPLUS
DOCUMENT NUMBER: 115:179579
TITLE: **Transport** of proteins towards the chloroplast thylakoid lumen
AUTHOR(S): Weisbeek, Peter; Hageman, Johan; De Boer, Douwe; Smeekens, Sjef
CORPORATE SOURCE: Inst. Mol. Biol., Univ. Utrecht, Utrecht, 3584 CH, Neth.
SOURCE: Isr. J. Bot. (1991), 40(2), 123-37
CODEN: IJBOAU; ISSN: 0021-213X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Many proteins found in the **chloroplast** are synthesized in the cytoplasm as transit peptide-contg. precursor mols. Stroma-targeted proteins have to cross the 2 envelope membranes; lumen proteins, however, have also to be transferred over the thylakoid membrane, i.e., they have to cross 3 biol. membranes in order to reach their final location. Recent evidence shows that the routing of plastocyanin (PC) towards the lumen involves 2 post-translational **transport** processes and is mediated by 2 different regions of the transit peptide. Concomitant with the **transport**, the transit peptide is removed in 2 successive steps. The transit peptide consists of 2 functionally different domains. The extent to which each domain is involved in import and routing and how far these 2 processes are **linked** is studied. The results show that the N-terminal part of the transit peptide is responsible for import into the **chloroplast**. The N-terminal 43 amino acids are sufficient to direct other proteins into the stroma. The C-terminal part of the transit peptide is a prerequisite for routing inside the **chloroplast** but not for import. Transgenic tomato plants that constitutively express a foreign PC gene were used to study protein **transport** into different tissues. Thus plastids of developmentally different tissues are capable of importing precursor proteins normally not found in these tissues. Most likely such plastids, though functionally and morphol. differentiated, have similar or identical protein import mechanisms when compared to the **chloroplasts** in green tissue. It is postulated that this **transport** mechanism evolved by the addn. of a **chloroplast**-specific targeting peptide to the **signal** peptide-contg. PC precursor of the endosymbiont, after the genetic information for this thylakoid protein had been transferred from the endosymbiont to the **nucleus**.

L14 ANSWER 26 OF 29 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1983:501042 CAPLUS
DOCUMENT NUMBER: 99:101042
TITLE: Mechanisms of citrate oxidation by Percoll-purified mitochondria from potato tuber
AUTHOR(S): Journet, Etienne Pascal; Douce, Roland
CORPORATE SOURCE: Dep. Rech. Fondam., Univ. Sci. Med. Grenoble, Grenoble, 38041, Fr.
SOURCE: Plant Physiol. (1983), 72(3), 802-8
CODEN: PLPHAY; ISSN: 0032-0889
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The mechanisms and accurate control of citrate oxidn. by Percoll-purified potato tuber mitochondria were characterized in various metabolic conditions by recording time-course evolution of citric acid cycle-related intermediates and O2 consumption. Intact potato tuber mitochondria showed good rates of citrate oxidn., provided that nonlimiting amts. of NAD and

thiamin pyrophosphate were present in the matrix space. Addn. of ATP increased initial [redacted]idn. rates, by activation of th[redacted]energy-dependent net citrate uptake, an[redacted]by stimulating succinate and ma[redacted]te formation. When the intramitochondrial NADH-to-NAD ratio was high, .alpha.-ketoglutarate only was excreted from the matrix space. After addn. of ADP, aspartate, or oxalacetate, which decreased the NADH-to-NAD ratio, flux rates through the Krebs cycle dehydrogenases were strongly increased, and .alpha.-ketoglutarate, succinate, and malate accumulated up to steady-state concns. in the reaction medium. Thus, the NADH-to-NAD ratio could be the primary **signal** for coordination of fluxes through the electron **transport** chain or malate dehydrogenase and NAD-**linked** Krebs cycle dehydrogenases. In addn., these results clearly showed that the tricarboxylic acid cycle could serve as an important source of C skeletons for extramitochondrial synthetic processes, according to supply and demand of metabolites.

L14 ANSWER 27 OF 29 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1983:67278 CAPLUS
DOCUMENT NUMBER: 98:67278
TITLE: Interrelationship between oxidative energy transformation and energy consumption at mitochondrial and cellular levels
AUTHOR(S): Letko, G.; Kuester, U.; Bohnensack, R.; Boehme, G.; Pohl, K.; Kunz, W.
CORPORATE SOURCE: Inst. Physiol. Chem., Med. Akad., Magdeburg, 3090, Ger. Dem. Rep.
SOURCE: Acta Biol. Med. Ger. (1982), 41(9), 735-50
CODEN: ABMGAJ; ISSN: 0001-5318
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The adaptation of oxidative energy transformation in **mitochondria** to the energy demand of cellular metab. was investigated in expts. with isolated **mitochondria** and liver cells and by computer simulation in terms of a math. model. Sep. draining of different energy pools allowed the detn. of the relation between these pools and the elucidation of the importance of the connecting enzyme reactions to the regulation of the whole process. The intramitochondrial adenine **nucleotide** pool exhibits a homogeneous behavior, and its changes are the **signal** for ATP synthesis. The protonmotive force which is in near-equil. with the intramitochondrial phosphorylation potential is the immediate **signal** for the respiratory chain. The intramitochondrial phosphorylation potential is transformed into the external potential by a flux-dependent nonequil. reaction of the translocator. The rate of respiration-**linked** ATP formation is regulated by >1 reaction step with varying control strength. In both isolated **mitochondria** and hepatocytes, an activation of respiration is provoked by a decrease in the **mitochondrial** energy state caused by cellular energy utilization.

L14 ANSWER 28 OF 29 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1981:187002 CAPLUS
DOCUMENT NUMBER: 94:187002
TITLE: Posttranslational **transport** of proteins in the assembly of mitochondrial membranes
AUTHOR(S): Neher, E. M.; Harmey, M. A.; Hennig, B.; Zimmermann, R.; Neupert, W.
CORPORATE SOURCE: Inst. Physiol. Chem., Univ. Goettingen, Goettingen, 3400, Fed. Rep. Ger.
SOURCE: Dev. Genet. (Amsterdam) (1980), 2(Organ. Expression Mitochondrial Genome), 413-22
CODEN: DEGNDX
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Neurospora Poly(A)+-RNA was incubated with reticulocyte lysates and Neurospora mitochondria to study the assembly of proteins into

mitochondria membranes. The 3 proteins studied were cytochrome c, the ADP/ATP carrier, and ATPase subunit 9. In all 3 cases, the proteins are translocated by a posttranslational mechanism, the intramitochondrial precursors differ in their properties from the functional products, and the precursors pass through the cytosolic compartment. The type of conformational change which leads to the final product apparently differs among the proteins. In the case of cytochrome c, the covalent **linkage** of the heme group within the mitochondrion leads to a drastic refolding of the mol. Refolding of the ADP/ATP carrier may occur in the step in which the precursor, bound to the outer membrane, is inserted into the inner membrane, whereas ATPase subunit 9 probably experiences a conformational change when the addnl. sequence is cleaved. Thus, the signaling device which directs a precursor protein to its organelle may lie in the tertiary, **signal** structure.

L14 ANSWER 29 OF 29 LIFESCI COPYRIGHT 2000 CSA
ACCESSION NUMBER: 1998:2780 LIFESCI
TITLE: RNA import elements for **transport** into mitochondria
CORPORATE SOURCE: UNIVERSITY OF TEXAS
SOURCE: (19961029) . US Patent 5569754; US Cl. 536/23.5 435/320.1.
DOCUMENT TYPE: Patent
FILE SEGMENT: W3
LANGUAGE: English

AB The invention relates to small RNAs encoded within the **nucleus** of mammalian cells that specifically import to the **mitochondria**. The RNAs bind to several **nucleolar** peptides and thus provide potential carriers for import of biological molecules, including metabolites and proteins, into the **mitochondrial** compartment. **Mitochondrial** dysfunction in several maternally inherited human diseases may be correctable employing **linkage** of **mitochondrial** import **signal** to **mitochondrial** tRNA sequences expressed from **nuclear** trans-genes without requirement for direct genetic transformation of **mitochondria**.